COMBINED USE OF FUROSEMIDE WITH SELECTIVE AND NONSELECTIVE β-ADRENERGIC ANTAGONISTS FOR TREATMENT OF EDEMATOUS SYNDROME ASSOCIATED WITH CHRONIC CIRCULATORY FAILURE IN RATS

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Nowadays, a viewpoint about the increased activity of renin-angiotensin and sympathoadrenal systems in patients with edematous syndrome due to circulatory failure is generally accepted. Activation of these humoral systems in case of congestive heart failure and in cases of number of other cardiovascular diseases causes homeostatic reaction of kidneys which accompanied by the increase of sodium reabsorption in nephron and water retention in organism. This effect partly is result of stimulation of β-adrenergic receptors of renal tubules and of juxtaglomerular cells producing renin. Therefore, it is possible that β-adrenergic antagonists can cause in such conditions diuretic and natriuretic reactions which may be used for correction of water and electrolyte disturbances in diseases accompanied by increased activity of sympathoadrenal system.

To test of this assumption, we had investigated the influence of nonselective β-adrenergic antagonist obzidan and β_1-adrenergic antagonist talinolol upon the specific diuretic effect of furosemide in rats. The chronic stenosis of inferior vena cava was used for the modeling of sodium retention. In 7–8 days after operation, the control trial had showed that the reliable increase of urinary excretion of creatinine was noted in rats with chronic stenosis of inferior vena cava in comparison with falsely-operated animals on the background of water load. But despite of an increased level of glomerular filtration, the quantity of urine had tended to certain reduction. In same time, the excretion of sodium and potassium had authentically decreased. Sodium retention on the background of increased glomerular filtration indicates about significant stimulation of sodium reabsorption in kidneys of rats with chronic stenosis of inferior vena cava. Administration of furosemide to animals was accompanied by specific diuretic and saluretic reactions due to inhibition of sodium and water reabsorption. Confirmation of this is level of creatinine which was practically unchanged. Simultaneously, the increase of potassium excretion with urine was observed.

Preliminary obzidian injection to rats with experimental sodium retention significantly influences character of kidneys reaction upon furosemide. In comparison with administration of furosemide alone, the reliable increase of urination and sodium and potassium excretion were observed in case of simultaneous use of both agents. Diuretic and natriuretic reactions had increased on 39 and 42% respectively. The quantity of excreted with urine creatinine was changed insignificantly, although there has been a tendency to the increase. Therefore, previous blockage of β_1- and β_2-adrenergic receptors with obzidan has promoted more significant inhibition of sodium and water transport in renal tubules by furosemide.

In the same time, findings of investigation of cumulative effect of furosemide and talinolol upon functional state of kidneys of rats with chronic stenosis of inferior vena cava testify that selective β_1-adrenergic antagonist talinolol has not significant influence upon functional changes in rats kidneys in response to furosemide. Difference between values of glomerular filtration, diuresis, sodium and potassium excretion in case of combined use of furosemide and talinolol was unreliable.

Thus, unlike of selective β_1-adrenergic antagonist talinolol, nonselective β-adrenergic antagonist obzidan increases diuretic and natriuretic effects of furosemide in rats with experimental retention of sodium which induced by chronic stenosis of inferior vena cava. This potentiating effect is due to a fact that the total blockage of β-adrenergic receptors significantly reduced sympathoadrenal influence upon kidneys. Therefore, there is reason to recommend the nonselective β-adrenergic antagonists for potentiating of therapeutic effect of diuretics in patients with edematous syndrome in diseases associated with activation of sympathoadrenal and renin-angiotensin systems.

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